REMARKS

The Office Action

Claims 1-53 are pending. Claims 1-11, 17, 19, 20, 23-48, 50, and 52 are under consideration. Claims 1-11, 17, 19, 20, 23-48, 50, and 52 stand rejected for indefiniteness and lack of written description. Claims 1-11, 17, 19, 20, 23-27, 33-36, 42-48, 50, and 52 stand further rejected for anticipation by Cai et al. (Proc Natl Acad Sci USA, 1995, 92:6537; hereafter "Cai"). Claims 1-11, 17, 19, 20, 23-27, 29-48, 50, and 52 stand rejected for obviousness over Cai in view of Hutchens et al. (U.S. Patent No. 6,225,047; hereafter "Hutchens"). Claim 28 stands rejected for obviousness over Cai in view of Hutchens and Cull et al. (Methods in Enzymology 182:147; hereafter "Cull").

Support for the Amendments

In general, the claims have been rephrased for clarity. The dependent claims have also been amended to be consistent with amendments to the independent claim. Claim 1 has been amended to include the limitations of claim 2. The species included in the first through sixth products recited in the claims have also been clarified, as depicted in Figures 1-6. Numerical identifiers have been added for the arrays and complex biological samples recited in the claims to aid in clarity and referencing in the dependent claims. Limitations that species in a library or product bind or do not bind to a support find support, for example, in claims 23-26. The limitation "one or more" arrays finds support, for example, in claims 48-53. Support for removal of the reference to first and second

types of individuals is found, for example, on page 5, lines 1-22 and page 10, lines 13-15. New claim 54 finds support in original claim 1. No new matter has been added.

The Invention

Prior to addressing the rejections raised by the Office, Applicant provides the following explanation of the invention. Amended claim 1, from which the remaining claims depend, recites:

> A method of identifying a polypeptide, said method comprising:
> (a) providing one or more first arrays comprising one or more polypeptides from a first complex biological sample adhered to a support;
> (b) providing one or more second arrays comprising one or more polypeptides from a second complex biological sample adhered to a support;
> (c) exposing a peptide-nucleic acid coupled library at least one time to one of said first arrays to create a first product comprising one or more species of said library that either (i) bind to said first array or (ii) do not bind to said first array;
> (d) exposing said first product at least one time to one of said second arrays to create a second product comprising one or more species of said first product that either (i) bind to said second array or (ii) do not bind to said second array;
> (e) exposing said peptide-nucleic acid coupled library at least one time to one of said second arrays to create a third product comprising one or more species of said library that either (i) bind to said second array or (ii) do not bind to said second array; and
> (f) exposing said third product at least one time to one of said first arrays to create a fourth product comprising one or more species of said third product that either (i) bind to said first array or (ii) do not bind to said first array,
> wherein the presence or absence of a species in said second or fourth product is indicative of the identity of a polypeptide that is present in said first and second complex biological samples, absent in said first and second complex biological samples, or not present in the same amount in said first complex biological sample compared to said second complex biological sample.

This method is exemplified in Figures 1-3, portions of which are reproduced below. Figure 1 illustrates steps (a) and (b) in which proteins (or polypeptides) from two samples are immobilized (or adhered) onto a column (or solid support). The capital letters in each column represent the amount and type of proteins bound to the column. In this example, the proteins in the two samples are not the same.

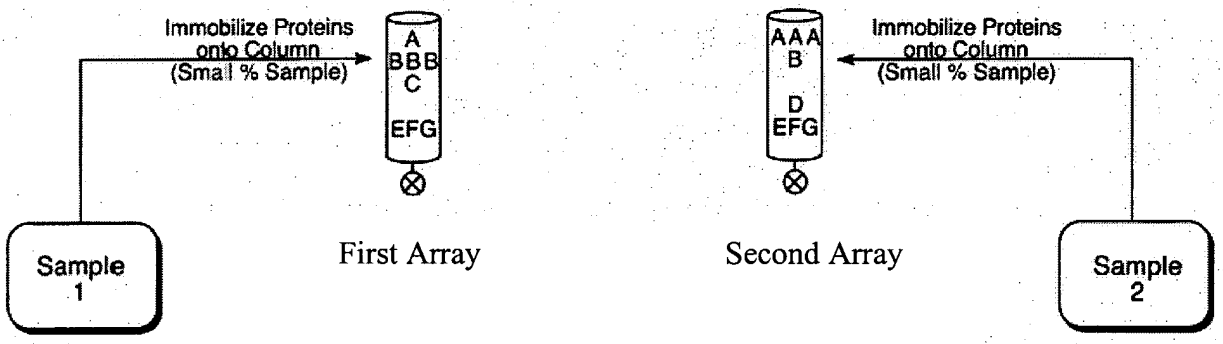


Figure 2 illustrates steps (c) and (e) in which a phage library (peptide-nucleic acid coupled library) is exposed to the columns provided in steps (a) and (b). In this example, the first and third products are phage that are first bound to the proteins in the columns and then eluted (lower case letters). Again, in this example, the phage that bind to each column are different because the proteins bound to the columns are different.

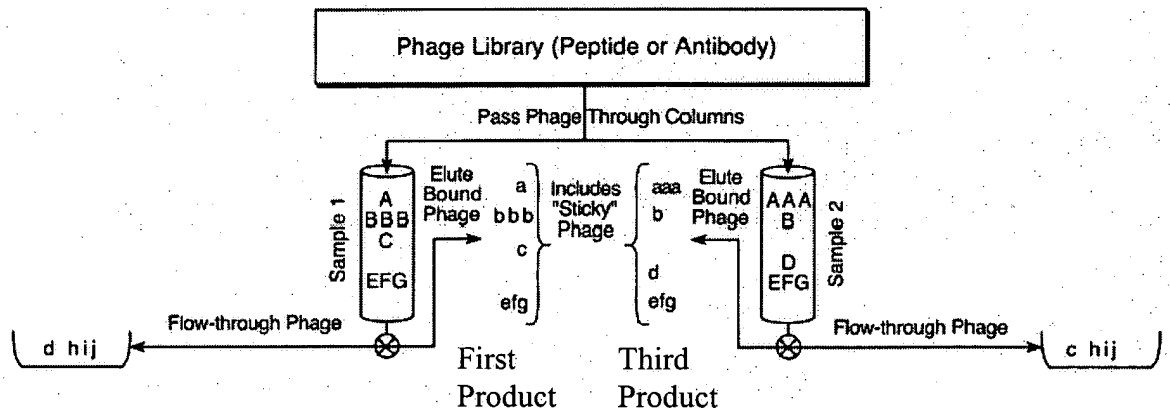
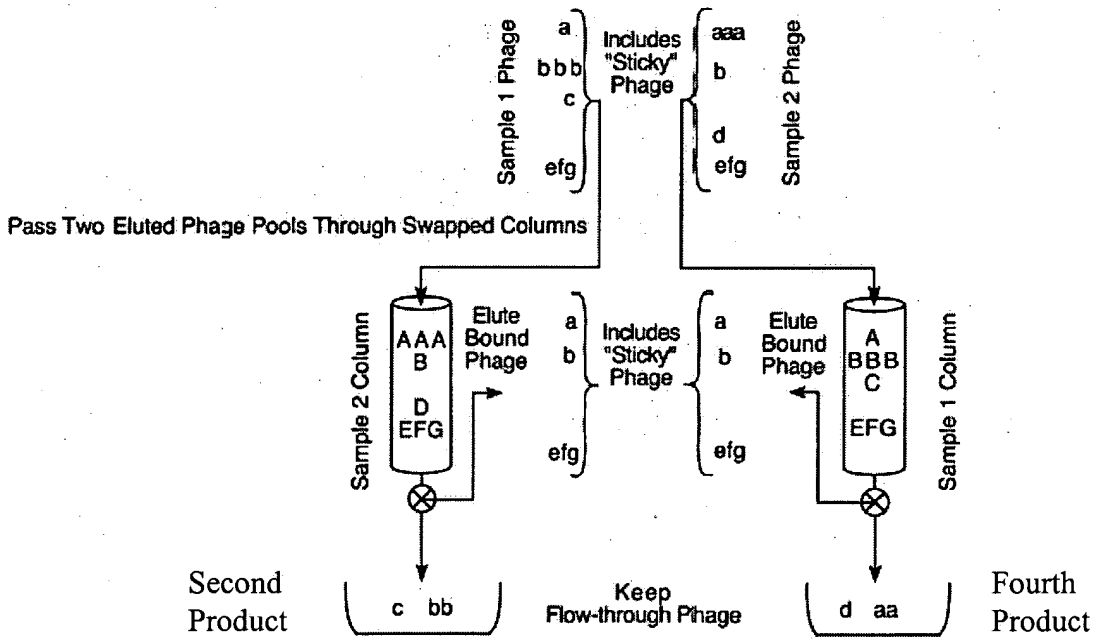


Figure 3 illustrates steps (d) and (f) in which the Sample 1 Phage (first product) and the Sample 2 Phage (third product) are contacted with the opposite column, i.e., the first product is contacted with the second column, and the third product is contacted with the first column. In this example, the phage that bind to one sample, but not the other, are the second (Flow-through phage from Sample 2 Column) and fourth (Flow-through phage from Sample 1 Column) products.



The presence or absence of a species in the second or fourth products is indicative of the identity of proteins that are present or absent in the first and second samples, or present in different amounts in the first and second samples. In this example, species in the second product indicate that Sample 1 contains proteins B and C in greater amounts than Sample 2, and species in the fourth product indicate that Sample 2 contains the proteins A and D in greater amounts than Sample 1.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-11, 17, 19, 20, 23-48, 50, and 52 stand rejected for indefiniteness. The purpose of the definiteness requirement is to ensure that "the scope of the claim is clear to a hypothetical person possessing the ordinary skill in the pertinent art" (M.P.E.P. § 2171).

The Office has rejected claim 1 for reciting "adhering a complex biological sample ... to a support to create an array." Claim 1 has now been amended to recite "one or more first arrays comprising one or more polypeptides from a first complex biological sample adhered to a support." Thus, the claim now requires that polypeptides in the complex biological sample be adhered to the support to create the array, and the method is complete.

The Office has also objected to recitation of first, second, third, fourth, fifth, and sixth products because "the metes and bounds of the chemical composition ... is unclear. Applicants have amended claims 1, 5, and 6 to clarify the composition of these products. With reference to the discussion of the invention above, the first product includes one or more species of a peptide-nucleic acid coupled library that either (i) bind to the first array or (ii) do not bind to the first array. The second product includes one or more species of the first product that either (i) bind to the second array or (ii) do not bind to the second array. The third product includes one or more species of the same library that either (i) bind to the second array or (ii) do not bind to the second array. The fourth product includes one or more species of the third product that either (i) bind to the first array or

(ii) do not bind to the first array. Thus, the first through fourth products include subgroups of molecules or molecular complexes, which are species from the same peptide-nucleic acid coupled library.

The fifth product includes one or more polypeptides from the first or second complex biological sample that either (i) bind to the third array (which includes one or more species from the second and fourth products) or (ii) do not bind to the third array. Finally, the sixth product includes one or more polypeptides from said first or second complex biological sample that either (i) bind to the third array or (ii) do not bind to the third array, where the complex biological sample utilized in this step of the method is different from that used to create the fifth product. Thus, the fifth product includes one or more polypeptides from one complex biological sample, and the sixth product includes one or more polypeptides from the other complex biological sample.

The amendments clarify the chemical composition of each of the first through sixth products, and the metes and bounds of these terms are clear.

Claim 1 was further rejected for omitting a step of identifying a polypeptide. Claim 1 has now been amended to recite how polypeptides are identified using the claimed method. The Office further rejected the claims for failing to recite a treating step. The instant methods may be employed without a treating step, and, as such, the omission of such a step in claim 1 is appropriate. Dependent claim 27 does recite an optional treating step, rendering the issue moot for this claim.

Applicants have amended the instant claims or provided arguments to address the indefiniteness rejections, and the rejection may be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-11, 17, 19, 20, 23-48, 50, and 52 stand further rejected for failing to comply with the written description requirement, in particular, with respect to three sets of terms: peptide-nucleic acid coupled library, types of individuals, and first through sixth products.

M.P.E.P. § 2163.02 states that "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.'" (citations omitted). Furthermore, M.P.E.P. § 2163 states:

> What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.... If a skilled artisan would have understood the inventor to be in possession of the the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, the adequate description requirement is met. (citations omitted)

Finally, a single disclosed species may be sufficient to adequately support a genus:

> disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered. (M.P.E.P. § 2163; citations omitted).

The instant claims meet these standards.

In rejecting the instant claims, the Office concludes that Applicant has failed to provide a recitation of structural features common to the members of the various genera or a representative number of species representative of the various genera. Other than this conclusion, the Office fails to provide any other reasoning to support the rejection. The genera at issue are peptide-nucleic acid coupled library, types of individuals, and first through sixth product.

Applicant first emphasizes that instant claims are directed to methods of identifying a polypeptide and not to compositions of matter per se. Such screening claims of this general type are routinely granted by the Office, when one reading the specification can comprehend and practice the claimed method. It is in some ways integral to the nature of such inventions that the products of such screens cannot be described in advance. The utility of the screen itself is in allowing characterization of the species identified by the screen.

As stated above, the claimed method employs a peptide-nucleic acid coupled library in the identification of polypeptides. The claimed methods are applicable to any complex biological sample, i.e., "any solid or fluid sample obtained from, excreted by, or secreted by any living organism" (specification, page 6, ll. 20-22) that may contain polypeptides.

With regard to "peptide-nucleic acid coupled library," the term refers to a common tool employed in the biological sciences. As recited in the instant claims, it is an agent through the use of which polypeptides in a sample may be identified. The specification

provides several examples of such libraries, including phage display libraries, and further provides a reference to review article on the general concept of display technology (Li et al. Nature Biotechnology 2000, 18:1251, of record). The specification also teaches that the peptide-nucleic acid coupled library "can be selected based on their particular properties, depending on the type of analysis required and the properties of the affinity reagents to be isolated" (pg. 15, ll. 3-5). Moreover, the exact nature of the peptide-nucleic acid coupled library is also not critical, as described in the specification on page 14, lines 12-19. It is indisputable that peptide-nucleic acid coupled libraries are known in the art, and one skilled in the art would recognize that Applicant had possession of use of this general tool for identifying polypeptides in a sample.

The facts of the instant case are also similar to that of Example 12 in the Revised Interim Written Description Guidelines Training Materials promulgated by the Office. In Example 12, the claim is directed to a process for identifying and selecting biological compounds that are present in a biological system. The specification in this Example indicates that obtaining the expression level is conventional in the art. The Example concludes that adequate written description is provided because "one skilled in the relevant art would understand what is intended by the claimed invention and know how to carry it out." In the present case, peptide-nucleic acid coupled libraries are conventional in the art, and their use to identify polypeptides in a sample is conventional in the art. Thus, one skilled in the art would understand what is intended in the instant claims, i.e.,

identification of polypeptides employing a peptide-nucleic acid coupled library, and know how to carry it out. This basis of the rejection may be withdrawn.

Regarding "types of individuals," this language has been deleted from the claims, and the rejection is now moot. As discussed above, the instant methods are applicable to the identification of polypeptides from any complex biological sample containing polypeptides. The specification provides a substantial list of sources for the complex biological sample, see, for example, page 6, line 20 to page 7, line 16 and page11, lines 8-26. From the breadth of the potential samples disclosed in the specification, it is clear that the source of the sample is not critical to the invention, and one skilled in the art would understand that Applicant's method is applicable to any such sample. Thus, Applicant was in possession of the claimed invention, and this basis of the rejection may also be withdrawn.

With respect to the first through sixth products, the claims have been amended to explicitly recite the type of chemical species that are included in these products. The first through fourth products include species from the same peptide-nucleic acid coupled library, the fifth product includes one or more polypeptides from one of the complex biological samples, and the sixth product includes one or more polypeptides from the other sample. The contents of each of these products will depend on the peptide-nucleic acid coupled library employed and the samples. As the samples vary, so will each of the products. Indeed, it is the contents of these products that are used to identify the polypeptides in the sample. Furthermore, as discussed above, the specification provides

guidance on the samples and peptide-nucleic acid coupled libraries that may be employed in the instant methods. One skilled in the art would understand that Applicant was in possession of each of these genera because each is produced during the method. This last basis of the rejection should also be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-11, 17, 19, 20, 23-27, 33-36, 42-48, 50, and 52 stand rejected for anticipation by Cai. In order to be anticipatory, a reference must teach every limitation of the claims (M.P.E.P. § 2131). Applicants traverse this rejection as applied to the amended claims.

The steps in claim 1 are outlined above. One key feature of the instant methods is that the same peptide-nucleic acid coupled library is first independently exposed to polypeptides from two samples. The product of the exposure with one sample is then exposed to the other sample. Thus, in the claimed method, polypeptides from two samples are contacted with an entire peptide-nucleic acid couple library and also with a subset of the peptide-nucleic acid library that either has affinity or does not have affinity to another sample. Cai simply does not teach such a method.

Cai teaches the following: a phage library is contacted with melanoma cells, and phage that bind to the melanoma cells are eluted and amplified. Thereafter, these eluted phage may be contacted with melanocytes, endothelial cells, and fibroblast cells to eliminate phage that cross react with healthy cells. Finally, individual phage identified by

the panning procedure may be tested for binding to a variety of cell lines. Thus, Cai only exposes the melanoma cells to a single phage library and members of the library that were eluted from the same melanoma cells. Cai does not expose the melanoma cells to phage eluted from another sample that was contacted with the entire phage library. Thus, nowhere does Cai teach exposing a peptide-nucleic acid library to two samples, and then exposing the product of that step, i.e., the first and third products, to the other sample, as instantly claimed.

Based on the foregoing, the anticipation rejection should be withdrawn. As Cai does not anticipate claim 1, it is unnecessary to consider the rejection of the dependent claims.

Rejections under 35 U.S.C. § 103

Claims 1-11, 17, 19, 20, 23-48, 50, and 52 stand rejected for obviousness over Cai in view of Hutchens or in view of Hutchens and Cull. Applicants traverse this rejection.

To support an obviousness rejection, the Office must put forth a *prima facie* case that meets the legal standard for obviousness found in M.P.E.P. § 2142. This section states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both

be found in the prior art, and not based on applicant's disclosure.

This standard has not been met in the present case as the combined references do not teach or suggest the instant claims.

In making the obviousness rejection, the Office acknowledges that it relies on Cai to teach the limitations of claim 1 and that Hutchens and Cai are only cited as teaching or suggesting limitations in the dependent claims. As stated above, Cai does not teach or suggest the limitations of claim 1. Furthermore, any teachings of Hutchens on using cross-linkers or mass spectrometry or of Cull on preliminary processing of biological samples do not remedy the deficiencies of Cai. Thus, the Office has failed to establish a *prima facie* case of obviousness, and the rejection should be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a petition to extend the period for reply for three months, to and including July 27, 2005. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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